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High Production Volume (HPV) Challenge Program

TEST PLAN
for
HEXAMETHOXYMETHYLMELAMINE

Melamine, hexakis(methoxymethyl)- (CAS # 3089-11-0)

Prepared by

HMMM Coalition

October 2002

A. INTRODUCTION

The HMMM Coalition has voluntarily agreed to provide information under the U.S. EPA HPV Initiative for melamine, hexakis (methoxy methyl)- (CAS # 3089-11-0), commonly known as hexamethoxymethylmelamine, and hereafter referred to as HMMM. By participating in this program, the Coalition has agreed to assess the adequacy of existing data on HPV endpoints, design and submit test plans to fill data gaps where necessary and appropriate, provide test results, and prepare summaries of the data characterizing HMMM.

HMMM is a methylated melamine formaldehyde resin used as a crosslinker in thermoset coatings such as beverage can coatings and automotive paint finishes. HMMM cannot be manufactured in pure form and cannot be isolated. Rather, it is contained in a polymer mixture, and the HMMM itself can be present within the mixture as a monomer (CAS No. 3089-11-0) or as a low-molecular-weight polymer. Commercial products usually contain about 28-50% HMMM. Thus, while certain properties can be estimated for a hypothetical 100% pure product, the test data presented here are from testing of commercial products containing HMMM. For the limited additional testing to be performed pursuant to this Test Plan, the HMMM Coalition will test a commercial product containing the highest amount of HMMM, approximately 50%.

The HMMM Coalition submitting this Test Plan consists of Borden Chemical, Inc., Cytec Industries Inc., and Solutia Inc. Solutia manufactures products containing HMMM in polymeric form, and hence is not covered by the HPV program. However, Solutia agreed to provide data regarding its HMMM-containing product. Its low-molecular-weight polymeric HMMM is very similar to the monomeric form of HMMM produced by Borden Chemical and Cytec Industries, and the data are representative of the CAS number listed in the HPV program.

Available data show HMMM has little or no toxicity to aquatic or mammalian organisms. Adequate data are available for almost all of the HPV endpoints:

- Data on physical and chemical properties, including melting point, boiling point, vapor pressure, partition coefficient and water solubility, are estimated from various models, assuming a 100% concentration of HMMM.

- With regard to environmental fate, HMMM is not predicted to be readily biodegradable, but it is expected to be inherently biodegradable. HMMM is estimated to have a half-life of minutes in sunlight. Fugacity modeling shows it most likely would be found in soil and to a lesser extent water, rather than air. Hydrolysis potential cannot be estimated from modeling, however, and no data are available on hydrolysis. Thus, the HMMM Coalition will test for hydrolysis.

- For the ecotoxicological endpoints, adequate data are available for acute toxicity to fish and invertebrates. In two separate tests of bluegill sunfish, no mortality was observed at any doses tested after 96 hours. Similarly, rainbow trout exposed to HMMM showed no mortality after 96 hours at any dose tested. A 48-hour test in daphnia magna also showed no mortality at any dose tested. ECOSAR modeling for daphnia magna produced estimates

similar to the bluegill sunfish experimental results. In short, HMMM is not toxic to aquatic organisms. There are no test data for algae, however, and the HMMM Coalition will undertake testing for this endpoint.

- Respecting the mammalian toxicity endpoints, adequate data exist on almost all of the endpoints, including acute toxicity, repeat dose toxicity, and genotoxicity. Multiple acute tests with oral doses show essentially no toxicity. A 28-day dermal repeat-dose test on HMMM is available. No effects were seen at 250 mg/kg/day, and no effects clearly related to treatment were seen at 750 and 1,000 mg/kg/day. The Ames test showed that HMMM is not mutagenic. While *in vitro* testing of Chinese hamster ovaries showed some effect, an *in vivo* chromosome aberration test was negative. Thus, HMMM is not considered clastogenic, and it displays little or no toxicity in mammalian studies.

- The only mammalian HPV endpoints for which data need to be generated for the HPV program are reproductive and developmental effects. Accordingly, the HMMM Coalition will undertake a combined reproductive/developmental test using OECD Protocol 422.

B. GENERAL SUBSTANCE INFORMATION

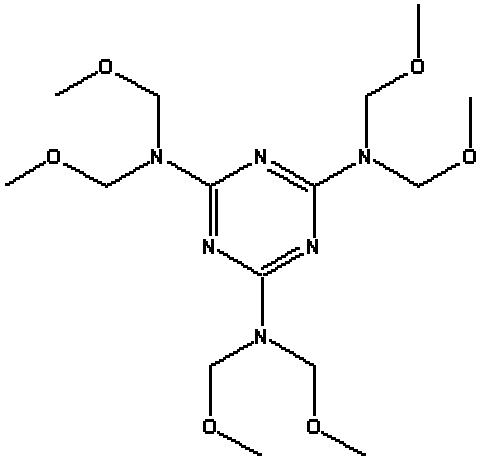
Chemical Name: Melamine, hexakis(methoxymethyl)-

HMMM is formed as a reaction product in addition to several other reaction products when melamine crystal is methylolated and methylated. HMMM does not exist as a pure material. It can exist in monomeric or polymeric form within a polymer mixture.

Chemical Abstract Service Registry Number: CAS # 3089-11-0

Common Name: HEXAMETHOXYMETHYLMELAMINE (HMMM)

Structural Formula: $C_{15}H_{30}N_6O_6$
Structure:



Molecular Weight: 390.44

Synonyms:
1,3,5-Triazine-2,4,6-triamine, N,N,N',N',N",N"-hexakis(methoxymethyl)-
Hexakis(methoxymethyl)melamine
Hexakis(methoxymethyl)melamin
hexakis(metoximetil)melamina Hexamethoxy methylmelamine
1,3,5-Triazine-2,4,6-triamine, N,N,N',N',N",N"-hexakis(methoxymethyl)-
2,4,6-[N,N-Bis(methoxymethyl)amino]-1,3,5-triazine
N,N,N',N',N",N"-Hexakis(methoxymethyl)-1,3,5-triazine-2,4,6-triamine
TRIAZINE [1,3,5]-2,4,6-TRIAMINE, N,N,N',N',N",N"- HEXAKIS(METHOXYMETHYL)-
HEXAMETHOXYMETHYL MELAMINE

Other Name(s):
1,3,5-Triazine-2,4,6-triamine, N,N,N',N',N",N"-hexakis(methyoxymethyl)-
Hexa(methoxymethyl)melamine
Hexamethyl methylolmelamine
Hexamethylolmelamine hexamethyl ether
Melamine, hexakis(methoxymethyl)-
N,N,N',N',N",N"-Hexakis(methoxymethyl)-1,3,5-triazine-2,4,6-triamine
Pidifix 330

C. MANUFACTURE AND DISTRIBUTION OF HMMM

Commercial methylated melamine formaldehyde resins are complex mixtures of dimers, trimers and higher oligomers. No direct industrial synthesis of HMMM has been reported. HMMM-containing resins are formed by methylolation of melamine with formaldehyde in the presence of acid or alkali, followed by methylation with methanol in the presence of acid.

HMMM containing resins are not sold directly to the consumer market. This material is reacted into the coatings in which they are added, limiting potential exposure in the finished consumer products.

HMMM is not sold as 100% HMMM. It is generally a mixture of HMMM and less methylolated/methylated species. The typical commercial form is either a solid wax or liquid at ambient temperatures. The solid wax can be heated back to liquid form.

D. USES OF HMMM

HMMM-containing resins are used as crosslinkers in thermoset coatings. Their principal function is to crosslink the molecules of the primary film-forming vehicle in a coating, in order to build a three-dimensional thermoset polymer network with high performance properties. This involves the reaction of the functional groups (such as the methoxymethyl groups on HMMM) to the complementary reactive groups on the vehicle, typically in the presence of an acid catalyst. This imparts characteristics such as hardness and mar resistance to the coating finishes. The thermoset coating formed from HMMM containing resins is considered excellent for solvent resistance, chemical resistance and exterior durability. Examples of applications are automotive

paint finishes and beverage can coatings. HMMM is also used in methylated melamine formaldehyde resins, which are approved by FDA for use in food packaging.

E. EXPOSURE INFORMATION

HMMM resin is the predominant crosslinking agent for thermoset coatings. Thermoset coatings undergo chemical reactions during the curing process so that the molecular weight is built up and crosslinking takes place. Thus, upon curing, the parent methylated melamine formaldehyde material is no longer present.

The only potential routine worker contact comes from sampling procedures for quality control, and in some instances, during packaging. Exposure would be by skin contact. Inhalation exposure is extremely low due to the use of ventilation and the material's low vapor pressure. Ingestion would not be expected.

No consumer exposure would be expected, as HMMM would not be present in the coated products.

F. SUMMARY OF AVAILABLE DATA AND TESTING TO BE UNDERTAKEN

Data on HMMM are already available for almost all of the HPV endpoints. The following paragraphs briefly summarize the available data, which are then presented in tabular form and in robust summaries.

Data on physical and chemical properties, including melting point, boiling point, vapor pressure, partition coefficient and water solubility, are estimated from various models, assuming a 100% concentration of HMMM. With regard to environmental fate, HMMM is not predicted to be readily biodegradable, but it is expected to be inherently biodegradable. HMMM is estimated to have a half-life of minutes in sunlight. Fugacity modeling shows it most likely would be found in soil and to a lesser extent water, rather than air. Hydrolysis potential cannot be estimated from modeling, however, and no data are available on hydrolysis. Thus, the HMMM Coalition will test for hydrolysis.

Commercial products containing HMMM have been tested for ecotoxicological endpoints and for mammalian endpoints.

For the ecotoxicological endpoints, adequate data are available for acute toxicity to fish and invertebrates. In two separate tests of bluegill sunfish, no mortality was observed at any doses tested after 96 hours. Similarly, rainbow trout exposed to HMMM showed no mortality after 96 hours at any dose tested. A 48-hour test in daphnia magna also showed no mortality at any dose tested. ECOSAR modeling for daphnia magna produced estimates similar to the bluegill sunfish experimental results. There are no data available evaluating potential toxicity to algae, however, and the HMMM Coalition will undertake such testing to fulfill this endpoint.

Respecting the mammalian toxicity endpoints, adequate data exist on almost all of the endpoints, including acute toxicity, repeat dose toxicity, and genotoxicity. Multiple acute tests with oral doses show essentially no toxicity. A 28-day dermal repeat-dose test on HMMM is available.

No effects were seen at 250 mg/kg/day. At 750 and 1,000 mg/kg/day, there were some effects on organ weights in males and liver enzyme values in females that were not clearly related to treatment. No clinical signs of dermal irritation or toxicity were observed. There were no macro or microscopic changes in any of the male or female reproductive organs.

The Ames test showed that HMMM is not mutagenic. Although *in vitro* testing of Chinese hamster ovaries showed some effect, an *in vivo* chromosome aberration test (bone marrow cytogenetics rat metaphase analysis) was negative. Thus, HMMM is not considered clastogenic, and it displays little or no toxicity in mammalian studies.

The only mammalian HPV endpoints for which data need to be generated for the HPV program are reproductive and developmental effects. Accordingly, the HMMM Coalition will undertake a combined reproductive/developmental test using OECD Protocol 422.
The tables below summarize the available data and the planned testing. The tables are followed by robust summaries of the existing data. A legend for the Klimisch codes is set out at the end of the robust summaries.

For the limited additional testing to be undertaken, the test material will be a Cytec Industries commercial product, consisting of approximately 50% HMMM. The remainder is a polymer of melamine, formaldehyde, and methanol (CAS# 68002-20-0). As noted above, HMMM cannot be produced in isolation. This commercial product is representative of the HMMM in commerce.

TABLE 1 SUMMARY OF AVAILABLE DATA ON HMMM

CAS# 3089-11-0	Study Date	Results	Data Acceptable
Physical/Chemical Characteristics*			
Melting Point	2002	**188.40 °C**	Yes
Boiling Point	2002	**448.20 °C**	Yes
Vapor Pressure	2002	**1.06 x 10^{-8} mm Hg @ 25 °C**	Yes
Partition Coefficient	2002	**Log K_{ow} = 1.61**	Yes
Water Solubility	2002	**149.3 mg/L @ 25 °C**	Yes
Environmental Fate*			
Photodegradation	2002	For reaction with hydroxyl radical, predicted rate constant = 323.5521 x 10^{-12} cm^3/molecule-sec **Predicted half-life = 23.802 minutes**	Yes
Hydrolysis		**No data**	**No Data**
Fugacity	2002	Predicted distribution using Level III Fugacity Model: **Air: 0.0000645%** **Water: 36.1%** **Soil: 63.8%** **Sediment: 0.0996%**	Yes
Biodegradation	2002	**Inherently biodegradable**	Yes
Ecotoxicity			
Acute Toxicity to Fish	 1993 1984 2002 1983	Lepomis macrochirus: **LC50 (96 hr) = 603.1 mg/L** **LC50 (96 hr) = >1,000 mg/L** LC50 (96 hr) = 673.2 (estimated) Salmo gairdneri: **LC50 (96 hr) = >1,000 mg/L**	 Yes Yes Yes Yes
Acute Toxicity to Invertebrates	 1983 2002	Daphnia magna **LC50 (48hr) = >1,000 mg/L** LC50 (48hr) = 702.2 mg/L (estimated by ECOSAR)	 Yes Yes
Acute Toxicity to Algae		**No data**	**No data**

Mammalian Toxicity			
Acute Toxicity			
Oral LD50 (rat)	2001	**oral LD50 (rat) = 2.0 g/kg**	Yes
Oral LD50 (rat)	1984	oral LD50 (rat) = 1.8 g/kg	Yes
Oral LD50 (rat)	1976	oral LD50 (rat) = 7.4 g/kg	Yes
Oral LD50 (rat)	1960	oral LD50 (rat) = >5 g/kg	No
Dermal LD50 (rabbit)	1976	**dermal LD50 (rat) = >7.9 g/kg**	Yes
Inhalation LC50	1976	6-hour inhalation LC50 = >0.6 mg/L	No
Primary Eye Irritation	1976	**Slight Eye Irritant**	Yes
Primary Skin Irritation	1976	Non-Irritating to Skin	No
Primary Skin Irritation	1988	**Mild to Non-Irritating to Skin**	Yes
Repeat Dose Toxicity			
28-Day Dermal (rat)	1990	**NOEL = 250 mg/kg/day (dermal)** **NOAEL = 1000 mg/kg/day**	Yes
Developmental Toxicity		**No data**	**No Data**
Reproductive Toxicity		**No data**	**No Data**
Genetic Toxicity:			
Gene Mutations	1988	**Negative**	Yes
Chromosomal Aberration			
In Vitro (CHO Cell Assay)	1989	Positive (In Vitro)	Yes
In Vivo (Bone Marrow Cytogenetics)	1989	**Negative (In Vivo)**	Yes

* Estimated by modeling for hypothetical 100% concentration of HMMM.

TABLE 2 SUMMARY OF TESTING

CAS # 3089-11-0	Data Available	Data Acceptable	Testing Required
Study	Y/N	Y/N	Y/N
Physical/Chemical Characteristics			
Melting Point	Y	Y	N
Boiling Point	Y	Y	N
Vapor Pressure	Y	Y	N
Partition Coefficient	Y	Y	N
Water Solubility	Y	Y	N
Environmental Fate			
Photodegradation	Y	Y	N
Hydrolysis	N	**No data**	**YES**
Fugacity	Y	Y	N
Biodegradation	Y	Y	N
Ecotoxicity			
Acute Toxicity to Fish	Y	Y	N
Acute Toxicity to Invertebrates	Y	Y	N
Acute Toxicity to Algae	N	**No data**	**YES**
Mammalian Toxicity			
Acute Toxicity	Y	Y	N
Repeat Dose Toxicity	Y	Y	N
Developmental Toxicity	N	**No data**	**YES**
Reproductive Toxicity	Y	**No data**	**YES**
Genetic Toxicity: Gene Mutations	Y	Y	N
Genetic Toxicity: Chromosomal Aberration	Y	Y	N